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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/511,245 | 07/26/2005 | Neil Russell Foster | HILLS1130 | 8721 |

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| EXAMINER | |
|---|---|
| THEODORE, MAGALI P | |

| ART UNIT | PAPER NUMBER |
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| 1791 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/511,245 | FOSTER ET AL. | |
| | Examiner | Art Unit | |
| | Magali P. Théodore | 1791 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-10,12-14,16-18,20-24,26-29 and 31-41* is/are pending in the application.

4a) Of the above claim(s) *20-24,26-29,31-38,40 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12-14,16-18 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/13/2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***Election/Restrictions***

1. Applicant's election of claims 1, 3-10, 12-14, 16-18, 27-29 and 39 in the reply filed on October 31, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 20-24, 26, 30, 31-38 and 40-41 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 31, 2008.

3. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group IA, claim(s) 1, 3-10, 12-14, 16-18 and 39, drawn to a method of making a pharmaceutical product.

Group IB, claim(s) 27-29, drawn to a treatment method.

4. The inventions listed as Groups IA and IB do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

5. The special technical features which link the claims of Groups IA and IB are the combination of a dense or liquefied gas with a substance to make a solution and then the formation of particles from said solution at lower pressure. Whether or not a technical feature makes a contribution over the prior art and therefore constitutes a "special technical feature" is considered with respect to novelty and inventive step. (MPEP [R-6] 1850 II.) As evidenced by Henriksen (WO 97/14407, p 3 paragraph 4), the claimed technical features are known in the art. Therefore, the special technical features fail to define a contribution over the prior art and unity of invention is lacking between these two groups.

6. During a telephone conversation with Ms. Lisa Haile on December 1, 2008 a provisional election was made without traverse to prosecute the invention of Group IA, claims 1, 3-10, 12-14, 16-18 and 39. Affirmation of this election must be made by applicant in replying to this Office action. Claims 27-29 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### *Drawings*

8. Figure 1 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

### *Specification*

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claim 18 recites that the encapsulated particles comprise "a mixture or combination of the substance and the polymer for sustained release applications." The specification discloses encapsulation with a polymer or with "a mixture or combination of a polymer and a relatively, [sic] biologically inert material for sustained release applications" [0024]. No teaching has been found of the concept that the biologically inert material itself is a polymer.

### *Claim Rejections - 35 USC § 112*

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**Claim 18** recites "the polymer." Claim 18 depends on claim 14, which depends on claim 1. Neither of claims 1 and 14 recites a polymer. For the sake of compact prosecution, "the polymer" has been interpreted as "a polymer."

## *Claim Rejections - 35 USC § 103*

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3-6, 8-12 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerč et al. (International Journal of Pharmaceutics, 182 (1999), pp 33-39, "Kerč") in view of Kropf et al. (US 6,316,030 B1, "Kropf").

Regarding **claim 1**, Kerč discloses a method of working with fenofibrate (page 34 left, last paragraph, line 3). Kerč teaches applying a liquefied gas (supercritical carbon dioxide, title) to a mixture of fenofibrate and a carrier (page 35 right, section 2.2 top) and heating the mixture close to but lower than the drug's atmospheric melting point (page 35 right, section 2.2 bottom) until the mixture is melted (page 35 right, section 2.2 line 2), producing a carrier fluid in contact with the molten drug. The entire mixture is within an autoclave (figure 1 at A) and therefore at the same pressure as the liquefied gas. Then the mixture is sent to a vessel of lower pressure (expansion chamber, figure 1 at C) where particles form.

Kerč does not positively state that the fenofibrate is solid before it meets the liquefied gas or that the liquefied gas melts the fenofibrate. However, Kropf teaches making particles by applying a liquefied gas (carbon dioxide, page 3 lines 16-19) to a solid substance ("melted by the introduction of gas," page 3 line 17) and then taking the solution to an environment of reduced pressure ("expansion through a nozzle") to form particles of the substance (page 3 lines 23-24). The melting point of the substance is depressed in the presence of the supercritical gas (page 3 lines 20). The step explicitly taught by Kropf is an effective alternative to melting the drug before introducing the liquefied gas. Therefore it would have been obvious to one of ordinary skill in the art to use the liquefied gas to melt solid fenofibrate in the method taught by Kerč, either by combining Kropf's teaching with the steps in Kerč's as they are explicitly disclosed or by substituting Kropf's melting step for a pre-melting step.

Regarding **claim 3**, Kerč does not explicitly teach that the carrier is the same as the liquefied gas. However, Kerč presents the carrier as optional (page 34 section 2.2 line 3) and shows the liquefied gas acting as a carrier fluid by carrying the drug into the expansion chamber (figure 1). Therefore, it would have been obvious to one of ordinary skill in the art to use the same gas as the liquefied gas and the carrier fluid because Kerč discloses the liquefied gas acting as a carrier fluid.

Regarding **claims 4-5**, Kerč teaches allowing the substance and the liquefied gas to equilibrate for about two hours before spraying (page 35 left lines 2-3). Kerč does not specify equilibrating *before* adding the carrier. However, selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected

results and selection of any order of mixing ingredients is prima facie obvious (MPEP 2144.04 IIC). Therefore it would have been obvious to one of ordinary skill in the art to equilibrate the drug and the liquefied gas for two hours before introducing the carrier because Kerč teaches both those steps.

Regarding **claim 6**, fenofibrate is a pharmaceutical agent (a hypolipidemic, Abstract).

Regarding **claim 8**, Kerč teaches that the temperature is between 5 ºC and 150 ºC (70 ºC, page 38 left line 6).

Regarding **claim 9**, Kerč teaches that the pressure of the liquefied gas and the carrier fluid is between 5 bar and 200 bar (190 bar, page 38 left line 6).

Regarding **claim 10**, Kerč teaches that the liquefied gas is carbon dioxide (title).

Regarding **claims 12-13**, Kerč does not teach the particle sizes specified by the claims. However, Kerč teaches that particle size determines the drug's dissolution rate and bioavailability. Therefore it would have been obvious to one of ordinary skill in the art to optimize the particle sizes in order to control the drug's dissolution and absorption by the body. Optimizing a result-effective parameter known in the art does not impart patentable distinction to an invention. See MPEP 2144.05 [R-5] II, in re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Regarding **claim 39**, Kerč teaches that the substance is fenofibrate (page 34 left, last paragraph, line 3).

15. Claims 7, 14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerč in view of Kropf as applied to claims 1 and 6 above, and further in view of Zhu et al. (US 2002/0110526 A1, "Zhu").

Regarding **claim 7**, Kerč does not teach applying this method to cyclosporine. However, Zhu teaches using supercritical fluid technology ([0059] lines 10-12) to make slow-release coated particles of cyclosporine ([0020] second-to-last line). Therefore, it would have been obvious to one of ordinary skill in the art to substitute cyclosporine for the fenofibrate taught by Kerč because Zhu teaches that cyclosporine is a suitable material to micronize by treating it with a liquefied gas.

Regarding **claims 14** and **16-18**, Kerč does not address encapsulation. However, Zhu teaches using supercritical fluid technology ([0059] lines 10-12) to encapsulate drug particles with biodegradable, slow-release polymers like poly(d,l-lactide-co-glycolide) ([0005] line 3] and cellulose ([0040] penultimate line) in order to preserve the drug as it makes its way into the body ([0004]). Therefore it would have been obvious to one of ordinary skill in the art to incorporate encapsulation with biodegradable slow-release polymers into the supercritical fluid method taught by Kerč because Zhu teaches doing so to preserve the activity of the drug.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magali P. Théodore whose telephone number is (571) 270-3960. The examiner can normally be reached on Monday through Friday 9:30 a.m. to 6:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina A. Johnson can be reached on (571) 272-1176. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Magali P. Théodore/
Examiner, Art Unit 1791

/Christina Johnson/

Supervisory Patent Examiner, Art Unit 1791